hereditary sensory and autonomic neuropathy type II

Hereditary sensory and autonomic neuropathy type II (HSAN2) is a condition that primarily affects the sensory nerve cells (sensory neurons), which transmit information about sensations such as pain, temperature, and touch. These sensations are impaired in people with HSAN2. In some affected people, the condition may also cause mild abnormalities of the autonomic nervous system, which controls involuntary body functions such as heart rate, digestion, and breathing. The signs and symptoms of HSAN2 typically begin in infancy or early childhood.

The first sign of HSAN2 is usually numbness in the hands and feet. Soon after, affected individuals lose the ability to feel pain or sense hot and cold. People with HSAN2 often develop open sores (ulcers) on their hands and feet. Because affected individuals cannot feel the pain of these sores, they may not seek treatment right away. Without treatment, the ulcers can become infected and may lead to amputation of the affected area. Unintentional self-injury is common in people with HSAN2, typically by biting the tongue, lips, or fingers. These injuries may lead to spontaneous amputation of the affected areas. Affected individuals often have injuries and fractures in their hands, feet, limbs, and joints that go untreated because of the inability to feel pain. Repeated injury can lead to a condition called Charcot joints, in which the bones and tissue surrounding joints are destroyed.

The effects of HSAN2 on the autonomic nervous system are more variable. Some infants with HSAN2 have trouble sucking, which makes it difficult for them to eat. People with HSAN2 may experience episodes in which breathing slows or stops for short periods (apnea); digestive problems such as the backflow of stomach acids into the esophagus (gastroesophageal reflux); or slow eye blink or gag reflexes. Affected individuals may also have weak deep tendon reflexes, such as the reflex being tested when a doctor taps the knee with a hammer.

Some people with HSAN2 lose a type of taste bud on the tip of the tongue called lingual fungiform papillae and have a diminished sense of taste.

Frequency

HSAN2 is a rare disease; however, the prevalence is unknown.

Genetic Changes

There are two types of HSAN2, called HSAN2A and HSAN2B, each caused by mutations in a different gene. HSAN2A is caused by mutations in the *WNK1* gene, and HSAN2B is caused by mutations in the *FAM134B* gene. Although two different genes are involved, the signs and symptoms of HSAN2A and HSAN2B are the same.

The *WNK1* gene provides instructions for making multiple versions (isoforms) of the WNK1 protein. HSAN2A is caused by mutations that affect a particular isoform called the WNK1/HSN2 protein. This protein is found in the cells of the nervous system, including nerve cells that transmit the sensations of pain, temperature, and touch (sensory neurons). The mutations involved in HSAN2A result in an abnormally short WNK1/HSN2 protein. Although the function of this protein is unknown, it is likely that the abnormally short version cannot function properly. People with HSAN2A have a reduction in the number of sensory neurons; however, the role that *WNK1/HSN2* mutations play in that loss is unclear.

HSAN2B is caused by mutations in the *FAM134B* gene. These mutations may lead to an abnormally short and nonfunctional protein. The FAM134B protein is found in sensory and autonomic neurons. It is involved in the survival of neurons, particularly those that transmit pain signals, which are called nociceptive neurons. When the FAM134B protein is nonfunctional, neurons die by a process of self-destruction called apoptosis.

The loss of neurons leads to the inability to feel pain, temperature, and touch sensations and to the impairment of the autonomic nervous system seen in people with HSAN2.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- congenital sensory neuropathy
- hereditary sensory and autonomic neuropathy type 2
- HSAN type II
- HSAN2
- HSAN2A
- HSAN2B
- HSANII
- HSN type II
- Morvan disease

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Hereditary sensory and autonomic neuropathy type IIA
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2752089/
- Genetic Testing Registry: Hereditary sensory and autonomic neuropathy type IIB
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2751092/

Other Diagnosis and Management Resources

- GeneReview: Hereditary Sensory and Autonomic Neuropathy Type II
  https://www.ncbi.nlm.nih.gov/books/NBK49247

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Degenerative Nerve Diseases
  https://medlineplus.gov/degenerativenervediseases.html
- Health Topic: Peripheral Nerve Disorders
  https://medlineplus.gov/peripheralnervedisorders.html

Genetic and Rare Diseases Information Center

- Hereditary sensory and autonomic neuropathy type 2
  https://rarediseases.info.nih.gov/diseases/3976/hereditary-sensory-and-autonomic-neuropathy-type-2

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Hereditary Neuropathies https://www.ninds.nih.gov/Disorders/All-Disorders/Hereditary-Neuropathies-Information-Page
- National Institute of Neurological Disorders and Stroke: Peripheral Neuropathy https://www.ninds.nih.gov/Disorders/All-Disorders/Peripheral-Neuropathy-Information-Page
- National Institutes of Health Rare Diseases Clinical Research Network: The Inherited Neuropathies Consortium http://www.rarediseasesnetwork.org/cms/inc/Healthcare-Professionals/CMT

Educational Resources

- Orphanet: Hereditary sensory and autonomic neuropathy type 2 http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=970
- University of Chicago Center for Peripheral Neuropathy http://peripheralneuropathycenter.uchicago.edu/

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) https://rarediseases.org/rare-diseases/hereditary-sensory-and-autonomic-neuropathy-type-ii/
- The Foundation for Peripheral Neuropathy https://www.foundationforpn.org/

GeneReviews

- Hereditary Sensory and Autonomic Neuropathy Type II https://www.ncbi.nlm.nih.gov/books/NBK49247

Scientific Articles on PubMed

- PubMed https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28hereditary+sensory+and+autonomic+neuropathy+type+ii%5BTIAB%5D%29+OR+%28HSAN2%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- NEUROPATHY, HEREDITARY SENSORY AND AUTONOMIC, TYPE IIA http://omim.org/entry/201300
- NEUROPATHY, HEREDITARY SENSORY AND AUTONOMIC, TYPE IIB http://omim.org/entry/613115

Sources for This Summary

- Axelrod FB, Gold-von Simson G. Hereditary sensory and autonomic neuropathies: types II, III, and IV. Orphanet J Rare Dis. 2007 Oct 3;2:39. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17915006
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2098750/
- Huang CL, Kuo E. Mechanisms of disease: WNK-ing at the mechanism of salt-sensitive hypertension. Nat Clin Pract Nephrol. 2007 Nov;3(11):623-30. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17957199
- Kurth I, Pamminger T, Hennings JC, Soehendra D, Huebner AK, Rotthier A, Baets J, Senderek J, Topaloglu H, Farrell SA, Nürnberg G, Nürnberg P, De Jonghe P, Gal A, Kaether C, Timmerman V, Hübner CA. Mutations in FAM134B, encoding a newly identified Golgi protein, cause severe sensory and autonomic neuropathy. Nat Genet. 2009 Nov;41(11):1179-81. doi: 10.1038/ng.464. Epub 2009 Oct 18.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19838196
- Lafreniere RG, MacDonald ML, Dube MP, MacFarlane J, O'Driscoll M, Brais B, Meilleur S, Brinkman RR, Dadivas O, Pape T, Platon C, Radomski C, Risler J, Thompson J, Guerra-Escobio AM, Davar G, Breakefield XO, Pimstone SN, Green R, Pryse-Phillips W, Goldberg YP, Younghusband HB, Hayden MR, Sherrington R, Rouleau GA, Samuels ME. Identification of a novel gene (HSN2) causing hereditary sensory and autonomic neuropathy type II through the Study of Canadian Genetic Isolates. Am J Hum Genet. 2004 May;74(5):1064-73. Epub 2004 Apr 1.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15060842
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1181970/
- Moriguchi T, Urushiyama S, Hisamoto N, Iemura S, Uchida S, Natsume T, Matsumoto K, Shibuya H. WNK1 regulates phosphorylation of cation-chloride-coupled cotransporters via the STE20-related kinases, SPAK and OSR1. J Biol Chem. 2005 Dec 30;280(52):42685-93. Epub 2005 Oct 31.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16263722
- Murphy SM, Davidson GL, Brandner S, Houlden H, Reilly MM. Mutation in FAM134B causing severe hereditary sensory neuropathy. J Neurol Neurosurg Psychiatry. 2012 Jan;83(1):119-20. doi: 10.1136/jnnp.2010.228965. Epub 2010 Nov 28.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21115472
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3721196/
- Shekarabi M, Girard N, Rivière JB, Dion P, Houle M, Toulouse A, Lafrenière RG, Vercauteren F, Hince P, Laganiere J, Rochefort D, Faivre L, Samuels M, Rouleau GA. Mutations in the nervous system--specific HSN2 exon of WNK1 cause hereditary sensory neuropathy type II. J Clin Invest. 2008 Jul;118(7):2496-505. doi: 10.1172/JCI34088.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18521183
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2398735/
- Verhoeven K, Timmerman V, Mauko B, Pieber TR, De Jonghe P, Auer-Grumbach M. Recent advances in hereditary sensory and autonomic neuropathies. Curr Opin Neurol. 2006 Oct;19(5):474-80. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16969157
- Verpoorten N, De Jonghe P, Timmerman V. Disease mechanisms in hereditary sensory and autonomic neuropathies. Neurobiol Dis. 2006 Feb;21(2):247-55. Epub 2005 Sep 23. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16183296

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/hereditary-sensory-and-autonomic-neuropathy-type-ii

Reviewed: May 2011
Published: March 21, 2017

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